Brucella abortus S19 genome sequenced; points toward virulence genes

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Researchers at the Virginia Bioinformatics Institute at Virginia Tech and the National Animal Disease Center in Ames, Iowa, and collaborators at 454 Life Sciences of Branford, Conn., have sequenced the genome of *Brucella abortus* strain S19. Strain S19 is a naturally occurring strain of *B. abortus* that does not cause disease and was discovered by Dr. John Buck in 1923. It has been used for more than six decades as vaccine that protects cattle against brucellosis, an infectious disease caused by other strains of *B. abortus* that leads to reproductive failure in livestock.

Scientists have long wanted to know what genetic features make strain S19 suitable for use as a vaccine in cattle because it may hold the secret as to why other Brucella strains cause disease and trigger the abortion of developing embryos in livestock. The researchers have discovered a group of 24 genes that are linked to virulence by making comparisons of the newly available S19 genome sequence to previously sequenced genomes of two virulent strains of *B. abortus*. The paper "Genome sequence of *Brucella abortus* vaccine strain S19 compared to virulent strains yields candidate virulence genes" was published recently in PLoS One (May 2008, Volume 3, Issue 5, e2193).

Oswald Crasta, project director at VBI's Cyberinfrastructure Group and the corresponding author on the paper, remarked: "We have been able to leverage rapid sequencing of the S19 genome on the Roche GS-20™ and GS-FLX™ platforms, and comparative genomics narrowed down the search for Brucella virulence factors to a small group of genes. Of particular interest are four genes that show consistently large sequence

differences in S19 compared with two fully sequenced virulent strains." He added: "Further studies are underway to characterize the short list of protein differences that appear to be involved in cellular processes ranging from lipid transport and metabolism to transcription and protein transport. We believe that this characterization will explain why strain S19 has been such a successful vaccine over the years and why infection with other strains leads to disease."

The initial sequencing was performed on the Roche GS-20™ at 454 Life Sciences, and subsequently repeated after the installation of the Roche GS-FLX™ in the VBI Core Laboratory Facility. Additional traditional sequencing methods were used in VBI's Core Laboratory Facility to completely finish the S19 genome sequence. Clive Evans, Associate Director of the Core Laboratory Facility at VBI, remarked: "The S19 sequence was the first bacterial genome sequenced at VBI with the new Roche GS-FLX™, which was installed in January 2007. The Roche GS-FLX™ sequence allowed us to verify and improve the original sequence, and reduced the number of gaps that needed to be covered with traditional sequencing methods. We were very pleased with the performance of the Roche GS-FLX™."

Bruno Sobral, Executive and Scientific Director of VBI and co-author, remarked: "The complete genome sequence of strain S19 helps us understand the causal molecular agents of brucellosis." He remarked: "Brucella is able to pass from animals to humans with relative ease and poses a significant public health burden for workers in the livestock industry. It is also a possible agent for agricultural, civilian and military bioterrorism. This emphasizes the need for researchers to have a handle on the genetic makeup of the different Brucella strains."

The manuscript is available on-line at
www.plosone.org/doi/pone.0002193